

10/02/1792
5060
(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
13 September 2001 (13.09.2001)

PCT

(10) International Publication Number
WO 01/66155 A3

(51) International Patent Classification⁷: **A61K 51/04**, 51/10

(21) International Application Number: PCT/US01/05927

(22) International Filing Date: 23 February 2001 (23.02.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/185,220 25 February 2000 (25.02.2000) US

(71) Applicants and

(72) Inventors: **MA, Dangshe** [US/US]; 13011 Twinbrook Parkway, Rockville, MD 20851 (US). **MCDEVITT, Michael, R.** [US/US]; Apartment 6A, 5644 Netherland Avenue, Bronx, NY 10471 (US). **SCHEINBERG, David, A.** [US/US]; 325 Central Park West, New York, NY 10025 (US). **SIMON, Jaime** [US/US], Route 1, Box 199-A, Angleton, TX 77515 (US). **KIEFER, Garry, E.** [US/US]; 114 Juniper Street, Lake Jackson, TX 77566 (US). **FRANK, R., Keith** [US/US]; 213 Pansy Path, Lake Jackson, TX 77566 (US). **GULYAS, Gyongyi** [US/US]; 305 Timbercreek Drive, Lake Jackson, TX 77566 (US).

(74) Agent: **KARADZIC, Dragan, J.**; The Dow Chemical Company, Intellectual Property, B-1211, 2301 N Brazosport Boulevard, Freeport, TX 77541 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
6 June 2002

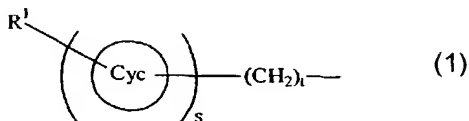
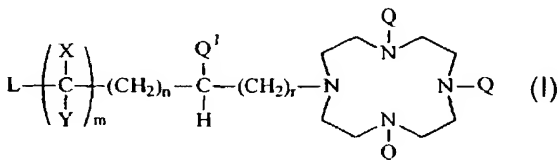
(15) Information about Correction:

Previous Correction:

see PCT Gazette No. 06/2002 of 7 February 2002, Section II

[Continued on next page]

(54) Title: ACTINIUM-225 COMPLEXES AND CONJUGATES FOR RADIOIMMUNOTHERAPY



(57) Abstract: Actinium-225 (²²⁵Ac) complexes with functionalized chelants of the formula (I) wherein: each Q is independently hydrogen or (CHR⁵)_pCO₂R; Q¹ is hydrogen or (CHR⁵)_wCO₂R; each R independently is hydrogen, benzyl or C₁-C₄ alkyl; with the proviso that at least two of the sum of Q and Q¹ must be other than hydrogen, each R⁵ independently is hydrogen; C₁-C₄ alkyl or (C₁-C₂ alkyl)phenyl; X and Y are each independently hydrogen or may be taken with an adjacent X and Y to form an additional carbon-carbon bond; n is 0 or 1; m is an integer from 0 to 10 inclusive; p is 1 or 2; r is 0 or 1; w is 0 or 1; with the proviso that n is only 1 when X and/or Y form an additional carbon to carbon bond, and the sum of r and w is 0 or 1; L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms to which it is joined, said linker/spacer group being represented by the formula (1) wherein s is an integer of 0 or 1; t is an integer of 0 to 20 inclusive; R¹ is an electrophilic or nucleophilic moiety which allows for covalent attachment to an antibody or fragment thereof, or

synthetic linker which can be attached to an antibody or fragment thereof, or precursor thereof; and Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not interfere with binding to an antibody or antibody fragment; with the proviso that when s, t, m, r, and n are 0, then R¹ is other than carboxyl; their pharmaceutically acceptable salts, their conjugates and the use thereof for radioimmunotherapy is disclosed.

WO 01/66155 A3